

DOUBLE PATENTING REJECTION

In the Office Action the Examiner rejected claims 1-3, 6-11, 13, 14, 23, 24, 27 and 28 based upon double patenting. Applicants have canceled claims 1-5, 8, 9, 17-22 and 27. Independent claim 6 has been amended to overcome the rejection, as discussed below. Claims 7 and 10-12 depend from the amended claim 6. Claims 23, 24 and 28 also depend from the amended claim 6. As such, Applicants request withdrawal of this rejection.

102 REJECTIONS

The Examiner rejected claims 1, 2 and 5-16 as being anticipated by Alberto, *et al.*, *J. Am. Chem. Soc.*, 1998, 120, pp. 7987-8. Of these claims, only independent claim 15 and dependent claim 16 remain pending in the application. The Examiner has argued that this reference discloses the ligand picolinamine-N,N-diacetic acid (PADA) and aminopolycarboxylic acid, as well as imino-N,N-diacetic acid. While the Examiner has correctly noted that aminopolycarboxylic acid is disclosed, the reference to PADA as shown in Scheme 2 also contains an aromatic pyridine, which is believed to be the relevant portion of the molecule useful in forming a stable Tc(I)-tricarbonyl complex. Moreover, Alberto states that imino-N,N-diacetic acid (IDA) portion of the molecule will not stabilize Tc(I). Rather, Alberto teaches that IDA will stabilize intermediate oxidation states of technetium, or those higher than Tc(I). Conversely, Applicant discovered that IDA stabilized Tc(I) quite well, in contrast to the teachings of the Alberto publication.

The Examiner has also rejected independent claim 15 based upon Alberto, *et al.* WO 98/48848. The Examiner has correctly noted that this reference discloses a method of preparing facial metal tricarbonyl compounds and using them to label biologically active substrates. The ligands suggested and disclosed in the reference have a tendency to stabilize metals in their low oxidation states. Such ligands commonly have the presence of low-lying vacant orbitals of the correct symmetry to form pi-bonds by accepting electrons from filled metal d-orbitals, a phenomenon known as "back bonding." The ligands disclosed in the cited reference include isonitriles, phosphines, thioethers, Schiff bases as well as pyridine, imidazole and pyrazole-type groups. In particular, the amino acid histidine is indicated as an ideal chelate. The difficulty with histidine and similar aromatic unsaturated organic molecules as chelates is that the resulting labeled compound is highly lipophilic, resulting in

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high liver and blood uptake. The hepatobiliary uptake and clearance are undesirable characteristics for targeting imaging agents.

Applicants' invention, in contrast, describes the use of non-aromatic aminocarboxylate ligands that were surprisingly discovered to form stable Tc(I) complexes. The resulting complexes have very desirable biological complexes such as low liver uptake and primary clearance via the kidneys. Because the cited reference neither discloses nor suggests the use of aminocarboxylate ligands, Applicants respectfully request withdrawal of the 102 rejection of the claims remaining in the application.

103 REJECTIONS

The Examiner rejected claims 1-3, 17, 19, 21-24 and 26-28 as obvious in light of the Alberto article. Of these, only dependent claims 23, 24, 26 and 28 remain pending in the application. These claims depend from amended claim 6. Applicant submits that this amendment, discussed above, places the claims in condition for allowance.

CONCLUSION

For the foregoing reasons, Applicants request allowance of the amended application.

Respectfully submitted,



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CERTIFICATE OF MAILING

I hereby certify that this Amendment (together with any documents referenced therein) is being deposited with the United States Postal Service (Express Mail) on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450.

Date: August 21, 2003


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